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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,635	08/09/2001	Nanna Kristensen Soni	4305/1H520US1	2913

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EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/925,635	Applicant(s) SONI ET AL.	
	Examiner Shanon Foley	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47 and 51-64* is/are pending in the application.

4a) Of the above claim(s) *3,21-57 and 60-64* is/are withdrawn from consideration.

5)☒ Claim(s) *17* is/are allowed.

6)☒ Claim(s) *1,2,4-16,18-20,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I as well as magnesium hydroxide, magnesium carbonate pentahydrate and/or titanium dioxide in paper No. 10 is acknowledged. The traversal is on the ground(s) that the instant compositions are not sufficiently distinct to warrant separate examination and searches. Applicant states that examples within the disclosure demonstrate that magnesium salt complexes in combination with various anions may function as effective vaccine adjuvants. Applicant requests that the claims be examined for generic salt complexes.

Applicant's arguments have been fully considered, but are found unpersuasive because each of the elements and complexes recited in the claims possess distinct molecular characteristics, properties and masses. These distinct physical properties are the basis for different functional characteristics that differentiate each element and complex. See MPEP § 806.04 and MPEP § 808.01. Since the adjuvant art is highly unpredictable, none of the elements or complexes presented are obvious alternatives to one another. Therefore, they are patentably distinct. After a review of examples 1 and 2 presented in the disclosure, it is noted that the examples do not encompass subject matter beyond what applicant has elected. The specific salts used in the examples as adjuvants are: magnesium hydroxide, magnesium carbonate pentahydrate and titanium dioxide, which are the elected salts. The claims will be examined to the extent they read upon the elected salt complexes.

The requirement is still deemed proper and is therefore made FINAL.

Claims 21-57 and 60-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Claim 3 is also withdrawn from further consideration because the claim encompasses compounds that are not commensurate in scope with the elected invention. Applicant timely traversed the restriction (election) requirement in Paper No. 9. Claims 1, 2, 4-20, 58 and 59 are under consideration.

Response to Amendment

The amendment filed 11/26/01 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is the statement "Each of these priority applications is incorporated herein, by reference in its entirety". The incorporation of these applications was not present when the instant application. Therefore, the incorporation of these applications subsequent to the instant filing date constitutes new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "Parenteral Vaccine Formulations with Inorganic Salt Adjuvants".

The disclosure is objected to because it lists "Rf" as a Group 4 element of the periodic table on page 3, lines 10 and 22 for example. However, this is not a recognized element within the standard Periodic Table. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-20, 58 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 lists "Rf" as a group 4 element. This is not a recognized element designation within the standard Periodic Table. Therefore, it is not clear which element applicant is intending to claim. This rejection also affects claims 2, 4-20, 58 and 59.

Claim 10 is confusing because it contradicts the limitations of claim 1. Claim 10 states that an additional adjuvant is selected from calcium phosphate and aluminum salts. However, claim 1 specifically requires that the adjuvant salt is not calcium phosphate. It is unclear how the parenteral vaccine formulation of claim 1 does not possess calcium phosphate, but comprises an additional adjuvant that is calcium phosphate. Claim 10 also states that the additional adjuvant is aluminum salts. However, the proviso of claim of claim 1 requires that magnesium hydroxide is not in combination with certain aluminum compounds. Although it is presumed that applicant intends for claim 10 to state that certain aluminum salts are excluded from the vaccine

formulation of claim 1 when the first adjuvant is magnesium hydroxide, the claim does not clearly reflect this concept. The additional "aluminum salts" recited in claim 10 includes those salts which are excluded from the vaccine formulation. Therefore, it is not clear whether applicant intends to exclude certain aluminum salts or not.

Claim 14 requires that the cation of the adjuvant is present in an amount from about 0.0004 to 120 M. The claim then provides an example of the amount claimed within the range. This example, denoted by "such as" does not provide further meaning to the claim and it cannot be determined whether the example is a further limitation of the amount of cation present or not. It is suggested that applicant delete the phrase "such...12M" from the claim or, if applicant intends for the more narrow range to be a further limitation, it is suggested that applicant draft a new claim reciting the more narrow range.

Claim 20 is also confusing for the same reasons discussed above regarding claim 10. Claim 20 states that an additional adjuvant is selected from calcium phosphate and aluminum salts. This claim directly depends from claim 16, which is drawn to magnesium hydroxide that cannot be combined with certain aluminum salt compounds. The additional "aluminum salts" recited in claim 20 includes those salts which are excluded from the vaccine formulation. Therefore, it is not clear whether applicant intends to exclude certain aluminum salts or not. Additionally, claim 20 states that the additional adjuvant is calcium phosphate, which is expressly excluded from the vaccine formulation in the preceding independent claim. Therefore, it is not clear whether applicant intends to exclude calcium phosphate or not.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-8, 11-13, 16, 58 and 59 are rejected under 35 U.S.C. 102(e) as being anticipated by Gonczol et al. (US 6,448,389).

Claims 1, 2, 4-8, 11-13, 58 and 59 are drawn to a parenteral vaccine formulation comprising at least one immunogenic substance and an adjuvant formed with a Group 2 element of the Period Table, i.e. magnesium hydroxide that is not combined with aluminum hydroxide or aluminum oxide. Claim 16 requires that the adjuvant is magnesium hydroxide. Claims 58 and 59 are drawn to methods of generating an immune response and vaccinating a subject by administering the instant vaccine formulation.

Gonczol et al. teach a vaccine formulation comprising DNA molecules expressing gB to induce immune responses to HCMV, see column 2, lines 22-27, column 4, line 63 to column 5, line 10. Gonczol et al. also teach suspending the DNA formulations in pharmaceutically acceptable carriers and incorporating a magnesium hydroxide adjuvant, see column 6, lines 31-41. Gonczol et al. also teach administering the composition by injection, see column 6, lines 42-63. Therefore, Gonczol et al. anticipate claims 1, 2, 4-8, 11-13, 16, 58 and 59.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 10 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al. as applied to claims 1, 2, 4-8, 11-13, 16, 58 and 59 above, and further in view of Vogel et al. ("A Compendium of Vaccine Adjuvants and Excipients" in Vaccine Design: The Subunit and Adjuvant Approach (Chapter 7), M.F. Powell & M.J. Newmann, Eds. (Plenum Press, New York) 1995, pp. 141-228), supplied by applicant in the IDS of paper no. 5.

The claims are drawn to the parenteral vaccine formulation comprising magnesium hydroxide and an additional adjuvant selected from known adjuvants such as Quil A, MPL and PLG.

See the teachings of Gonczol et al. above. Although the reference does not teach or suggest additionally adding a recited adjuvant in the claims, the references teaches that more than one adjuvant may be added to the composition, see column 6, lines 39-40.

Vogel et al. provide a brief summary of known adjuvants. These include MF59, MPL, PLGA and Quil A, see pages 183, 186-187, 198-199, and 210, respectively.

One of ordinary skill in the art at the time the invention was made would have been motivated to add conventional adjuvants to the composition of Gonczol et al. ensure boosting the immune response to the antigen. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for combining the adjuvants of Vogel et al. into

the composition of Gonczol et al. because Gonczol et al. teach that the composition may comprise more than one adjuvant and Vogel et al. review adjuvants well known in the art. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 1, 2, 4-8, 11-13, 18, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aviram et al. (US 6,362,236) and Conte et al. (US 5,464,633).

See the summary of claims 1, 2, 4-8, 11-13, 58 and 59 above. Claim 18 requires that the adjuvant is titanium dioxide.

Aviram et al. teach compositions and methods of administering a hydrolated cholesterol lowering agent, see claim 1 and examples 1-4 in columns 7-14. Aviram et al. teach that the hydrolated compounds are formulated for parenteral administration, as well as common excipients and carriers, such as titanium dioxide, see column 14, lines 8-13.

Although Aviram et al. do not teach that titanium dioxide is an adjuvant, Conte et al. specifically identifies titanium dioxide as an adjuvant by stating that "titanium dioxide and other adjuvants well known to the skilled in the field, may be used", see column 6, lines 17-18. Therefore, the adjuvanting property of titanium dioxide is well known in the art.

Neither reference teaches combining or administering titanium dioxide in a vaccine formulation. However, it is notoriously conventional in the vaccine art to administer art-recognized adjuvants in vaccine formulations to boost an immune response against a target antigen. Therefore, combining the art-recognized adjuvant, titanium oxide, in a vaccine formulation would have been prima facie obvious to one of ordinary skill in the art at the time

the invention was made with a reasonable expectation of success, absent evidence to the contrary.

Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al. as applied to claims 1, 2, 4-8, 11-13, 16, 58 and 59, or alternatively Aviram et al. and Conte et al. as applied to claims 1, 2, 4-8, 11-13, 18, 58 and 59 above.

Claims 14 and 15 require that the cation of the adjuvant composition is present in an amount ranging between about 0.0004 to 120 M or about 0.008 to 6 M.

See the teachings of Gonczol et al. or Aviram et al. and Conte et al. above. None of the references teach the concentration of the cation recited in the claims. However, each set of references teach using the claimed salts in compositions that are parenterally administered, which would necessarily comprise a molar concentration of cation within each composition. In addition, it is conventional practice in the vaccine arts to optimize the amount of components within a composition for individual administrations. Therefore, each concentration within the recited molar range of cations would have been prima facie obvious alternatives to one another to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al. as applied to claims 1, 2, 4-8, 11-13, 16, 58 and 59 above, and further in view of Aviram et al. and Conte et al.

The claim is drawn to a parenteral vaccine formulation comprising a combination of magnesium hydroxide and titanium dioxide.

See the teachings of Gonczol et al., Aviram et al. and Conte et al. above. None of the references teach combining titanium dioxide and magnesium hydroxide.

As evidenced by the teachings in the references, both compounds are known in the art to be adjuvants. Both Gonczol et al. and Conte et al. teach that the composition may comprise more than one adjuvant, see column 6, lines 39-40 of Gonczol et al. and column 6, lines 17-18 of Conte et al. Therefore, combining known adjuvants would have been prima facie obvious to one of ordinary skill in the art. Combining compounds, each possessing an adjuvanting effect, would necessarily produce a composition having an adjuvanting effect. There is no evidence in the specification that the combination of known adjuvants would have an unexpected result, i.e. synergism. Therefore, combining known adjuvants would have been accomplished with a reasonable expectation of success. The invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Allowable Subject Matter

The prior art does not teach or suggest that magnesium carbonate hydroxide pentahydrate is an adjuvant. Beckett (US 6,328,997) teaches preventing and treating clinical signs of influenza by administering a magnesium carbonate solution, see example 7 in column 40, lines 44 to column 41, line 31 and example 10, in column 44, lines 34-58. The magnesium carbonate solution is magnesium carbonate hydroxide pentahydrate administered parenterally, see column 13, lines 16-25 and lines 41-43, column 14, line 62-66, column 16, lines 10-13 and column 18, lines 41-45. However, Beckett does not teach or suggest that the magnesium carbonate hydroxide pentahydrate is an adjuvant. Therefore, claim 17 is drawn to allowable subject matter.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
June 12, 2003